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Bertoli, S ; Probst, R ; Bodmer, D

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Second revision

Authors:

Sibylle Bertoli^a, Rudolf Probst^b, Daniel Bodmer^a

Affiliations:

^a Department of Otorhinolaryngology, University Hospital Basel, Petersgraben 4,
CH-4031 Basel, Switzerland

E-mail: sbertoli@uhbs.ch, dbodmer@uhbs.ch

^b Department of Otorhinolaryngology, University Hospital Zürich,
Frauenklinikstrasse 24, CH-8091 Zürich, Switzerland

E-mail: rudolf.probst@usz.ch

Corresponding author:

Sibylle Bertoli

Department of Otorhinolaryngology

University Hospital

Petersgraben 4

CH-4031 Basel

Switzerland

Tel: +41 61 265 2042

Fax: +41 61 265 3883

E-mail: sbertoli@uhbs.ch

Abstract

This study investigated the effects of long-term unilateral and bilateral amplification on central auditory processing in elderly people with symmetrical hearing loss using late auditory evoked potentials. It was hypothesized that in the unilateral setting stimulation of the aided ear would yield an acclimatization effect with larger amplitudes and shorter latencies of the components P1, N1 and P2 compared to those of the unaided ear. Auditory evoked potentials were elicited by 500, 1000 and 2000 Hz pure tones at 55, 70 and 85 dB SPL presentation level delivered either to the left or right ear. Unilaterally and bilaterally fitted experienced hearing-aid users and a control group of normally hearing adults, all aged at least 60 years, participated. The responses of the unilateral hearing-aid users did not differ significantly for any of the components P1, N1 or P2 between the aided and unaided ears, but a significant interaction between ear and frequency was present for P2 amplitudes. P2 amplitudes were significantly smaller for the 0.5- and 1-kHz stimuli and tended to be larger for the 2-kHz stimulus in the aided ear suggesting an acclimatization effect. Larger P2 amplitudes were observed in the unilaterally fitted group, which was interpreted as a correlate of more effortful auditory processing in unilaterally fitted people.

Keywords: Acclimatization, AEP, auditory evoked potentials, bilateral, deprivation, hearing aids; P2, unilateral

Abbreviations: ABR, auditory brainstem response; AEP, auditory evoked potential; ANOVA, analysis of variance; DLF, discrimination limen for frequency; DLI, difference limen for intensity; ENT, ear nose and throat; ISI, interstimulus interval; PTA, pure tone average; S/N ratio, signal-to-noise ratio; SPIN, speech perception in noise; ULL, uncomfortable loudness level.

27 **Introduction**

28 Hearing aids may be fitted to one ear only or to both ears. Bilateral provision has
29 become the standard for people with symmetrical hearing loss, because two hearing
30 aids are thought to be superior to one for most individuals. The possible benefits of
31 bilateral fitting comprise better speech understanding (Kobler et al., 2002; Moore et al.,
32 1992), in particular in noisy environments (Dreschler et al., 1994; Leeuw et al., 1991;
33 Nabelek et al., 1981), better sound quality (Balfour et al., 1992; Erdman et al., 1981),
34 better sound localization (Byrne et al., 1992; Dreschler et al., 1994; Kobler et al., 2001;
35 Punch et al., 1991; Stephens et al., 1991), and improved perception of distance and
36 movement (Noble et al., 2006). Principles of acoustics and hearing physiology also
37 support the use of bilateral fitting.

38 Furthermore, when a hearing aid is fitted in people with bilateral hearing loss to only
39 one ear, a large subset of people experience auditory deprivation in the unaided ear,
40 which is manifested as a significant reduction in speech recognition performance in the
41 unaided ear over time (Gelfand et al., 1987; Silman et al., 1984). This effect appears in
42 general after two to three years of deprivation (Arlinger et al., 1996). In the aided ear,
43 by contrast, an acclimatization effect may be observed, which was defined as an
44 improvement in auditory performance that cannot be attributed to training effects only
45 (Arlinger et al., 1996). During the Eriksholm workshop on auditory deprivation and
46 acclimatization, areas for future research for a better understanding of this
47 phenomenon were identified (Arlinger et al., 1996; Neuman, 1996). One of the
48 suggestions was to use electrophysiological and imaging techniques to understand the
49 anatomical and physiological changes underlying the mechanisms of deprivation and
50 acclimatization. Objective measures of the effects of bilateral versus unilateral fittings
51 on auditory processing may also be desirable, because clinical field studies have failed
52 to show a clear advantage of bilateral fitting (Noble et al., 2006).

Gatehouse (one of the workshop participants) and Robinson (1996) investigated acclimatization to unilateral hearing-aid use in a single long-term user using simple electrophysiological measures. The subject was a 69-year-old man who had been aided in the right ear for 4 years with an average daily use of 8 hours. Auditory evoked potentials (AEPs) were acquired for 500 and 2000 Hz sinusoids at three presentation levels (65, 80, 95 dB SPL) for the aided and unaided ear separately. The composite average of the N1-P2 amplitude was measured. For the lower frequency there was no difference in N1-P2 amplitude between the ears at all levels, but for the 2000-Hz stimulus, the aided ear had a larger amplitude for the 95 dB SPL presentation level. The authors concluded that these results support a potential acclimatization effect induced by the hearing aid and that future research could use more refined electrophysiological measures to investigate changes induced by unilateral fitting.

Despite the suggestions of the Eriksholm workshop, studies using electrophysiological measures to investigate the potential deprivational effects of unilateral hearing-aid use are scarce. Munro et al. (2007a) investigated ear asymmetry in the auditory brainstem response (ABR) of long-term unilateral hearing-aid users (minimum experience 2 years, self-reported daily use >5 hours) and a group of people with symmetric high-frequency sensorineural hearing loss prior to hearing-aid fitting. Clicks were presented unilaterally at 70, 80 and 90 dB HL. Wave V amplitudes were higher for the 70 and 80 dB levels in the aided ear compared to the unaided ear, which was interpreted as an acclimatization effect at the brainstem level.

Hutchinson and McGill (1997) used P300, a discriminatory potential that is elicited in an oddball paradigm by a rare stimulus presented randomly among a sequence of frequent stimuli, to investigate auditory deprivation in ten unilaterally aided children aged 9 to 18 years (mean 13.1 years). These children had bilateral congenital severe to profound sensorineural hearing loss and had worn their aid for at least 8 years.

Stimuli (1000 Hz frequent, 250 Hz rare) were presented at a comfortable listening level (varying between 80 and 118 dB nHL) for each subject. The P300 amplitude was significantly greater in the aided ear compared to the unaided ear. Thus, the few studies that used electrophysiological measures to investigate the effects of unilateral hearing-aid use all reported increased amplitudes in the aided ear compared to the unaided ear. Interestingly, this increase was observed across the whole range of evoked potentials from ABRs to P300.

Evidence for acclimatization in unilateral hearing-aid users also comes from studies investigating speech perception, intensity discrimination and loudness perception (for a review, refer to Munro 2008). For example, Gatehouse (1989) used a speech-perception-in-noise test, with a group of unilaterally fitted adults. He found better performance at high presentation levels and poorer performance at low presentation levels for the aided ear compared to the unaided ear. Intensity discrimination was used by Robinson and Gatehouse (1995, 1996) to investigate acclimatization following unilateral fitting. The difference limen for intensity (DLI) was measured at 0.25 and 3 kHz. In the aided ear, the DLI for the 3-kHz stimulus was better at high presentation levels and poorer at low presentation levels. These results correspond to the findings of Gatehouse (1989) regarding speech perception. Another measure used to investigate acclimatization is the determination of uncomfortable loudness levels (ULL). Gatehouse and Robinson (1996) and Munro et al. (2007b) found a greater tolerance of loudness in the aided ear at higher frequencies (2 and 4 kHz). To summarize, all of these studies present converging evidence that unilateral hearing-aid use improves perception in the aided ear at high presentation levels, whereas performance at low presentation levels tends to decrease. This effect was observed only for higher frequencies (≥ 2 kHz) and for speech stimuli.

The current study was conducted for two purposes. First, we wanted to investigate the

effects of long-term unilateral hearing-aid use on late auditory evoked potentials. As a first exploratory approach and using a study design similar to that of the case study by Gatehouse and Robinson (1996), late AEPs comprising the P1-N1-P2 complex were measured in a group of unilateral hearing-aid users. We hypothesized that unilateral fitting would alter the responses. Specifically, we expected larger amplitudes and shorter latencies of either all or some of the components P1, N1 and P2, when the stimuli were presented to the aided ear compared to the responses from the unaided ear.

A second purpose was to examine differences in amplitudes and latencies of P1, N1 and P2 across a group of unilateral hearing-aid users, age-matched bilateral hearing-aid users and normal-hearing controls. These results are reported first. The nature of this investigation was exploratory and no specific hypotheses were advanced.

Materials and methods

Participants

Ten elderly bilateral hearing-aid users (mean age = 69.5 years, range 65-75 years; eight men), 10 unilateral hearing-aid users (mean age = 77.1 years, range 73-86 years; seven men) and a control group of 10 normal-hearing subjects (mean age = 70.1 years, range 66-73 years; 6 men) participated in the study. The unilateral users were significantly older than the bilateral users ($t=4.58$; $p<0.001$) and the normal-hearing subjects ($t=4.79$; $p<0.001$). Of the unilateral hearing-aid users, five wore their aid in the right ear and five in the left ear. Given the small subsample size, loss of hemispheric asymmetry, another potential consequence of unilateral amplification described in people with unilateral hearing loss, was not addressed in our study. As asymmetry seems to be affected differently by input from left and right ears (Hanss et al., 2009; Hine and Debener, 2007; Thai-Van et al., 2009), the study did not have enough power

for this type of investigation. Only long-term hearing-aid owners with regular use, defined as a total duration of at least 5 years and a daily self-reported use of ≥ 8 hours per day, were included. The average duration of hearing-aid use was 6.3 years (SD 1.9 years, range 5-11 years) for the unilateral group and 12.4 years (SD 7.3 years, range 5-30 years) for the bilateral group. There was a significant difference of 6.1 years in hearing-aid use duration between the two groups ($t=2.56$; $p<0.001$).

All hearing-aid users had digital aids with nonlinear signal processing features fitted by professional hearing-aid dispensers according to the Swiss hearing-aid dispensing system (Bertoli et al., 2009). No information about the real-ear insertion gain, i.e. the difference between aided and unaided ear canal sound pressure level, was available. However, the mean hearing threshold differences between 2 and 1 kHz were 18.3 dB (SD 9.5 dB) and 16.3 dB (SD 10.9 dB), and between 2 and 0.5 kHz 22.0 dB (SD 12.2 dB) and 21.3 dB (SD 12.8 dB) for the right and left ear, respectively. It can therefore be assumed that the hearing-aid gain was higher at 2 kHz compared to 0.5 and 1 kHz.

The hearing-impaired participants had a moderate high-frequency sensorineural hearing loss with a pure-tone average (PTA) at 0.5, 1, 2, and 4 kHz between 40 and 60 dB HL. Hearing thresholds did not differ significantly between unilateral and bilateral hearing-aid users. Hearing loss had to be symmetrical with a PTA difference between left and right ears not exceeding 10 dB. No significant differences between the hearing thresholds of right and left ears were found for any of the frequencies in both hearing-impaired groups (p -values between 0.09 and 0.84). Otoscopy and acoustic immittance testing were used to control for conductive hearing loss. The normal-hearing group had a PTA of 20 dB HL or better in both ears. The mean pure-tone audiograms of the three groups for the right and left ears are depicted in Figure 1. In addition, all subjects passed a screening test for dementia using a German version of the neuropsychological assessment battery of the Consortium to Establish a Registry for

Alzheimer's Disease (CERAD-NAB) with normative values adjusted for gender, age, and education (Thalmann et al., 2000; Welsh et al., 1994).

Hearing-aid users were recruited among participants of a prior study (Bertoli et al., 2010; Bertoli et al., 2009), from local hearing-aid dispensers and from the ENT-department of the University Hospital Basel. The normal-hearing subjects had either participated in prior studies or were recruited from a local longitudinal study on healthy aging. The study was approved by the local Ethics Committee of Basel and Baselland (EKBB) and all participants gave written informed consent prior to testing.

Speech audiometry

Two measures of speech perception were used to investigate whether perceptual evidence for acclimatization had occurred in the aided ear compared to the unaided ear in the unilateral hearing-aid users. The 50% correct speech recognition for monosyllabic words was determined using the Freiburger Einsilbertest (Hahlbrock, 1953). A modified German version of the speech-perception-in-noise (SPIN) test was administered using the sentences with low predictability to determine the signal-to-noise (S/N) ratio for which 50% of the final words of sentences presented in a constant background noise are correctly identified (Kalikow and Stevens, 1977; Tschopp and Züst, 1994). For the normal-hearing control group, the noise level was set at 60 dB SPL. For the hearing-impaired participants, the noise level was calculated by adding 30 dB to the 50% speech recognition score.

Stimuli and electrophysiological procedure

The stimuli were 0.5, 1 and 2 kHz pure-tones with a duration of 100 ms and a 10-ms rise/fall time. They were presented at 55, 70 and 85 dB SPL via ER3 insert earphones

either to the right or left ear, resulting in a total of 18 conditions (3 frequencies x 3 levels x 2 ears). Stimuli were delivered with an interstimulus interval (offset-to-onset) of 1s in two separate blocks of 900 stimuli each. Each block contained 50 presentations of each stimulus type and the order in which the stimuli were presented varied between the two blocks. Thus, each stimulus type was presented 100 times. The duration of one test block was about 20 min.

Recordings were conducted in a sound-treated and electrically shielded room. Participants were instructed to ignore the sounds and to concentrate on reading a text of their own choice.

EEG recording and averaging

The EEG was recorded using a Neuroscan Quicktrace system and disposable surface silver electrodes at Fz, Cz, Pz, left and right mastoids (LM, RM) according to the International 10/20 system, and at two lateral sites halfway between Fz - LM and Fz - RM, respectively (L1, R1). An electrode placed at the tip of the nose served as the reference and a forehead electrode as ground. Vertical eye movements were monitored with two electrodes attached above and below the left eye. Impedance was kept below 5 k Ω and controlled between the two test blocks.

The EEG (band pass 0.05 – 100 Hz) was recorded continuously at a sampling rate of 500 Hz and stored for off-line averaging. An ocular artifact reduction algorithm was used to reduce contamination by eye movements. Epochs containing 100-ms pre-stimulus and 500-ms post-stimulus time were obtained, baseline-corrected with respect to the pre-stimulus interval, and averaged by stimulus type. Epochs containing artifacts exceeding ± 100 μ V were rejected from averaging. The AEP waves were band-pass filtered at 0.1 – 20 Hz (24 dB/octave slope).

207

208 ***Electrophysiological data analysis***

209 For each subject, events corresponding to each condition were averaged. Grand mean
210 average waveforms were calculated for each subject group and stimulus type. The P1,
211 N1 and P2 peak amplitudes and latencies were measured in the waveforms at Cz,
212 where the largest potentials were seen, and at Pz, because there were clear responses
213 in the unilateral group that were less prominent or absent in the other two groups. The
214 composite N1-P2 amplitude was also calculated. The latency windows for the peak
215 measurements were determined based on the grand average waveforms (P1: 20-90
216 ms, N1: 40-170 ms, P2: 120-340 ms). In addition, to account for the sustained and
217 double-peaked P2, two mean amplitude voltages were measured for the 130 - 240 and
218 the 240 – 350 ms latency ranges (mean P2_{early} and mean P2_{late}, respectively). To
219 correct for multiple comparisons (two electrode sites), alpha level was adjusted to
220 <0.025.

221 Data were analyzed using SPSS software (version 19). The P1, N1 and P2 amplitudes
222 and latencies were analyzed using separate repeated-measures ANOVAs for electrode
223 sites Cz and Pz with subject group as the between-subject factor (unilateral, bilateral,
224 normal) and ear (left, right), frequency (0.5, 1, 2 kHz), and level (55, 70, 85 dB SPL) as
225 within-subject factors. Huynh-Feldt corrections were used where an assumption of
226 sphericity was not appropriate. When significant main effects were found for subject
227 group or interactions, Bonferroni's post-hoc measures were performed (alpha level
228 <0.05). Significant main effects for frequency and level were not further investigated
229 with post-hoc analyses, since the effects of these parameters on AEPs have been
230 studied extensively in the past (for a review, see Crowley and Colrain, 2004; Hyde,
231 1997) and were not of specific interest for the purpose of the current study.

232 To investigate the effect of hearing-aid use on AEPs, the ears of the unilateral group

were classified as aided and unaided. For bilateral users, ears were classified as left and right. Difference values for the two ears were calculated for all parameters (P1, N1, P2 amplitudes and latencies). For the unilateral group, results for the unaided ear were subtracted from those of the aided ear, for the bilateral group right ear results were subtracted from those of the left ear. Repeated-measures ANOVAs were then calculated for the difference values with factors subject group (unilateral, bilateral), frequency and level. The group with normal hearing was not included in this analysis. To investigate differences between aided and unaided ears in the unilateral group further, repeated-measures ANOVAs were performed with factors ear, frequency and level for N1 and P2 amplitudes and for the composite N1-P2 amplitude to enable a direct comparison of our results with those of the case study by Gatehouse and Robinson (1996). This analysis was performed for the unilateral group only.

Results

Speech audiometry

The results of the 50% speech discrimination and SPIN tests are listed in Table 1. For the normal-hearing and bilateral groups, results are reported for left and right ears, for the unilateral group for aided and unaided ears. The hearing-aid users' performance was significantly poorer on both tests compared to the normal-hearing people (p -values <0.001). Speech performance of the aided and unaided ears of the unilaterally fitted group was compared to each ear (right and left) of the bilaterally fitted group. None of the comparisons for the 50% speech discrimination and S/N ratio reached significance (p -values between 0.09 and 0.95). In the unilateral group, the 50% speech discrimination scores between aided and unaided ears did not differ significantly ($p=0.105$), although there was a trend towards better scores for the unaided ear. For the SPIN test, the S/N ratio was significantly better in the aided ear compared to the

unaided ear ($p=0.012$). In the bilateral and normal-hearing groups, no significant differences were noted between right and left ears for any of the speech tests.

AEP results

Comparison by subject group

Visual inspection of the waveforms

Figure 2 displays the responses to the 0.5 kHz stimulus presented at 85 dB SPL to the left ear at all eight electrode sites. Figure 3 depicts the grand mean average waveforms of the three subject groups for all 18 conditions at electrode sites Cz and Pz. For the normal-hearing group, the typical P1-N1-P2 complex was present for all frequencies and intensity levels at electrode site Cz. The hearing-aid users had clear responses for all stimulus types except the 2 kHz-tone presented at 55 dB SPL. For most hearing-impaired participants, this stimulus was below their hearing thresholds. At Pz, the group with unilateral hearing-aid provision had clearly visible responses for the 0.5 and 1 kHz stimuli, in particular at 70 and 85 dB SPL presentation level, whereas the responses were considerably reduced or absent in the bilateral and normal groups. At the lowest presentation level, the normal-hearing participants had larger N1 amplitudes compared to the hearing-impaired participants, whereas at the higher levels only minor differences for the P1 and N1 components could be noted. A pronounced and sustained P2 was found in the responses of the unilateral group compared to the bilateral and normal groups, who had generally smaller P2s. This effect was more pronounced at Pz. In some of the waveforms, P2 was double-peaked.

Amplitudes

Table 2 presents the results of the repeated-measures ANOVAs performed for P1, N1,

and P2 peak amplitudes and latencies and P2 mean voltages. There was a significant main effect of subject group at Pz on P2 peak amplitude and on the early portion of the mean P2 voltage, but not on N1 amplitude. Post-hoc analyses indicated that the unilateral group had significantly larger amplitudes than the bilateral group (P2 peak: $p=0.009$; mean P2_{early}: $p=0.007$). The means of the individual P2 amplitudes are plotted in Figure 4 for electrode sites Cz and Pz.

There was a significant main effect of level on the amplitudes of all components (P1, N1, P2), indicating larger amplitudes for the higher stimulus levels. Frequency affected N1 and P2 amplitudes and the mean P2_{early} significantly, indicating smaller amplitudes for higher frequencies. No significant interactions of subject group with ear, frequency and level were observed for any of the AEP components.

Latencies

There was a significant main effect of subject group on P1 latency at Cz. Both groups of hearing-aid users had longer latencies compared to the normal group (unilateral 47 ms, bilateral 49 ms, normal 42 ms). Post-hoc tests revealed that the differences were significant only for the bilateral group ($p=0.014$). There was also a trend towards a significant group effect on N1 latency at Cz ($F(2,27)=3.59$; $p=0.041$) with prolonged latencies for the two hearing-aid user groups (unilateral 105 ms, bilateral 108 ms, normal 100 ms). P2 latency was not affected significantly by subject group.

Frequency affected P1 and N1 latencies at Cz and Pz, whereas level affected N1 latency at Cz and P2 latency at Pz significantly. Again, no significant interactions of subject group with ear, frequency and level were observed for any of the AEP components.

Effects of unilateral vs. bilateral fitting

Figure 5 depicts the responses for all frequencies and levels for the two hearing-aid user groups at electrode site Cz. For the bilateral group, results are plotted for the right and left ear, whereas for the unilateral group results are plotted for the aided and unaided ear. In Figure 6, the means of the individual peak amplitudes and latencies are displayed for P1, N1 and P2.

Repeated measures ANOVAs showed a significant main effect of frequency on P2 amplitude differences between the two ears at Cz. For the frequencies 0.5 and 1 kHz, the average amplitude difference values were negative (-0.25 and -0.40 μV), whereas for 2 kHz the difference value was +0.25 μV . Post-hoc tests indicated a significant difference between the frequencies 1 and 2 kHz ($p=0.001$). There was no significant main effect of group and level nor was there an interaction between the factors for any of the parameters investigated indicating that unilateral hearing-aid use did not affect the responses differently compared to bilateral use. Table 3 summarizes the results of the repeated measures ANOVAs.

Despite the lack of a significant main effect of subject group, visual inspection of the plots for the mean P1, N1 and P2 amplitudes in Figure 6 revealed diverging trends for P2 amplitudes of aided and unaided ears in the unilaterally fitted group not observed in the bilaterally fitted group. Divergence increased with increasing presentation level in a frequency-specific manner. For the 0.5-kHz and 1-kHz stimuli, P2 amplitudes appeared larger in the unaided ear, and for the 2-kHz stimulus, P2 amplitudes appeared larger in the aided ear. To investigate these trends further, additional ANOVAs were performed for the unilateral group alone with factors ear, frequency and level. For comparison purposes with the study of Gatehouse and Robinson (1996), the ANOVAs were also performed for the composite N1-P2 in addition to N1 and P2 amplitudes. Results are given in Table 4. There was a significant main effect of level (at Cz and Pz) and of

frequency (Cz only), but not of ear, and there was a significant interaction between ear and frequency for P2 peak amplitude (at Cz) and for the composite N1-P2 amplitude (at Pz). Post-hoc tests revealed that P2 amplitudes were significantly larger in the unaided compared to the aided ears at the frequencies 0.5 kHz ($p=0.044$) and 1 kHz ($p=0.026$), but P2 tended to be smaller in the unaided ear at 2 kHz ($p=0.170$). The composite N1-P2 amplitudes were significantly larger in the unaided ear for the 1-kHz stimulus ($p=0.020$).

The trend for a larger P2 amplitude in the aided ears at 2 kHz is consistent with the larger N1-P2 amplitude in the aided ear at the same frequency reported in the case study of Gatehouse and Robinson (1996). Unlike Gatehouse and Robinson (1996), we found also an acclimatization effect at the lower frequencies of 0.5 and 1 kHz with significantly larger P2 amplitudes in the unaided ears. Our results also show that the acclimatization effect is related to changes in P2 amplitude and not in N1 amplitude.

Discussion

This study examined the hypothesis of an acclimatization effect on electrophysiological measures in the aided ear of experienced unilateral compared to bilateral hearing-aid users and a normal-hearing control group. In the unilateral group, no significant differences in P1, N1 and P2 amplitudes and latencies were found between the responses obtained separately from the aided and unaided ears. There was, however, a significant interaction between ear and frequency with smaller P2 amplitudes for the 0.5- and 1-kHz stimuli and a trend towards larger P2 amplitudes for the 2-kHz stimulus in the aided ear. Using speech audiometry, significantly lower S/N ratios for the aided ear compared to the unaided ear were demonstrated. Thus, the current study provides some electrophysiological and perceptual evidence for an acclimatization effect in the aided ears of unilateral hearing-aid users.

A comparison of the AEPs between unilateral and bilateral hearing-aid users and a group of elderly normal-hearing people revealed no significant findings except for larger P2 amplitudes in the unilateral group compared to the bilateral group, and longer P1 and N1 latencies in both hearing-aid groups compared to the normal-hearing group, but this increase was significant only for the bilaterally fitted group.

Acclimatization effects on late AEPs with unilateral hearing-aid use

An acclimatization effect of unilateral amplification has been reported using electrophysiological measures with widely different latencies such as short latency ABR and long latency P300 (Hutchinson and McGill, 1997; Munro et al., 2007a). Munro et al. (2007a) reported larger wave V amplitudes in the aided ear compared to the unaided ear. Investigating the effect of bilateral hearing-aid fitting on ABR, Philibert et al. reported significantly shortened wave V latencies only in the right ear, but not in the left ear after 3 and 6 months of regular bilaterally used hearing aids (Philibert et al., 2005). These ABR results suggest that acclimatization effects may occur at the initial more peripheral stages of central auditory processing. However, in both ABR studies only a small number of participants were tested (eight and five, respectively) and significant results were inconsistent and limited to either amplitude or latency of wave V or to one side only.

Hutchinson and McGill (1997) reported significantly greater P300 amplitudes in the aided ears of unilaterally aided children. Although these children had worn their hearing aids for at least 8 years, methodological differences preclude a direct comparison. First, the children had congenital severe to profound hearing loss. Second, at the age of 9 to 17 years long latency AEPs are still subject to maturational changes. Third, the P300 is a discriminative potential that requires attention to the stimuli.

Our study can be compared more readily to the results of Gatehouse and Robinson (1996). These authors reported a potential acclimatization effect in a single subject for the highest presentation level of the 2-kHz stimulus with larger N1-P2 amplitudes for the aided ear, but not for the 0.5-kHz stimulus. As Gatehouse and Robinson had measured the composite N1-P2 amplitude, it is unknown whether this difference was related to changes in N1, P2, or both. In the current study, we found a significant interaction between ear and frequency in the unilateral group for P2 and the composite N1-P2 amplitude, but not for N1. Inspection of Figures 5 and 6 revealed diverging trends for P2 in the aided and unaided ears with increasing levels, depending on the test frequency, whereas no such trends can be noted for N1. The results of the current study are consistent with the results of Gatehouse and Robinson (1996) for the 2-kHz stimulus and suggest that the changes are specifically due to an increase in P2 amplitude. In addition, unlike Gatehouse and Robinson (1996), who did not find differences between aided and unaided ears for the 0.5-kHz stimulus, our results extend the finding of an acclimatization effect to the lower frequencies of 0.5 and 1 kHz with larger P2 amplitudes at higher levels in the unaided ear. This means that acclimatization occurs at higher presentation levels at the frequencies to which the ear is most exposed: the unaided ear to the lower frequencies, and the aided ear to the higher frequencies. The fact that similar changes are not present in the bilaterally fitted group suggests that the changes are related to the asymmetry in the listening conditions across ears in the unilateral group.

The frequency specificity of the P2 enhancement with larger amplitudes in the unaided ear at 0.5 and 1 kHz and larger amplitudes in the aided ear at 2 kHz could also be interpreted as a mild form of representational plasticity. Responsiveness to the edge frequencies of dead regions has been reported for neurons adjacent to such regions. It is possible that with presbycusis, neural resources previously tuned to high-frequency

input become responsive to lower frequency input. Some evidence of such changes following gently sloping hearing losses have been reported in animal models (e.g., Frisina and Rajan, 2005). Moreover, several studies in humans have demonstrated that patients with steeply sloping sensorineural hearing loss exhibit an improvement in frequency discrimination performance at or around the cut-off frequency (McDermott et al., 1998; Thai-Van et al., 2002, Thai-Van et al., 2007). Following the introduction of a hearing aid, it might be that the neural resources shift back to respond to higher frequency input once more. This would explain the larger P2 amplitudes for low frequencies in the unaided ear and the larger P2 amplitudes for high frequencies in the aided ear. Gabriel et al. (2006) have demonstrated the existence of such a secondary plasticity induced by auditory rehabilitation. The discrimination limen for frequency (DLF) was investigated at the frequency with the best DLF before and at 1, 3 and 6 months following hearing-aid fitting. The DLF of the best frequency decreased significantly, while remaining stable at other frequencies. This change was interpreted as a central reorganization induced by amplification and reversing the initial hearing-loss induced changes in the cortical maps.

Speech audiometry in unilateral and bilateral hearing-aid users

When speech performance was compared between the ears of unilateral and bilateral long-term hearing-aid users, no significant differences were found. When the ears were compared within the unilateral group alone, S/N-ratios were significantly better for the aided compared to the unaided ear, but not speech discrimination scores. Thus, some audiometric evidence of acclimatization in unilateral hearing-aid users could be noted. Whether the worse S/N ratio in the unaided ear represents simply the lack of acclimatization or an additional deprivation effect (= deterioration compared to performance before wearing a hearing aid), cannot be deduced from our study due to

its cross-sectional design. The SPIN-test was presented to the hearing-impaired subjects at constant noise levels above 80 dB SPL (see Table 1). Our results are in line with those of Munro and Lutman (2003), who reported an acclimatization effect after 12 weeks of hearing-aid use, when using speech in noise at the highest presentation level of 69 dB SPL, but only minimal for 55 and 62 dB SPL. Gatehouse (1989) also reported that the aided ears performed better only at high presentation levels (>75 dB SPL), while at lower presentation levels the unaided ear was advantaged. The lack of a significant difference between aided and unaided ears for the speech discrimination test might therefore be related to the lower presentation levels between 53 and 57 dB SPL (see Table 1). Alternatively, the SPIN-test representing a more complex listening situation might be better suited for revealing acclimatization and deprivation effects than simple speech discrimination tasks.

P1 and N1 latency increase in hearing-aid users

The hypothesis that deprivation should cause changes in AEPs is partially based on the finding that sensorineural hearing loss is associated with a prolongation of latencies of the P1 and N1 components, occasionally also of P2 (Bertoli et al., 2005; Korczak et al., 2005; Oates et al., 2002; Polen, 1984; Tremblay et al., 2003). Oates et al. (2002) tested adults with hearing losses ranging from mild to severe and found prolonged ERP latencies with even mild hearing loss, whereas amplitudes were affected only in participants whose average hearing loss exceeded 60 dB HL. They suggested that any sensorineural hearing loss results in an overall slowing of the timing of the cognitive processes.

In accordance with these findings, the two groups of participants with symmetrical hearing loss and hearing-aid use showed a prolongation of the latencies of P1 and N1 compared to the normal-hearing group, but not of P2. The finding that P2 latency was

not significantly prolonged despite the latency increases of the preceding components P1 and N1 could be related to the sustained P2 latency range with a large variability of P2 peak amplitude measures.

P2 enhancement in unilateral hearing-aid users

A significantly larger P2 amplitude at Pz was found in the unilateral group in our study compared to the bilateral group. Unlike the N1 component of the late AEPs, the P2 component has not received much attention in the past, because it was considered to reflect the same neural mechanisms as the preceding N1 (Crowley and Colrain, 2004). As a consequence, data analysis was frequently limited to N1 or the composite N1-P2 amplitude and little is known about the functional significance of P2. Interpretations of P2 findings in the literature are frequently of a speculative nature. In a review, Crowley and Colrain (2004) documented that P2 can be dissociated from N1 experimentally, developmentally and topographically. An enhanced P2 has been reported from other areas of research, such as sleep (Crowley et al., 2002), dyslexic children (Ceponiene et al., 2009), and from auditory discrimination training (Alain and Snyder, 2008; Atienza et al., 2002; Bosnyak et al., 2004; Reinke et al., 2003; Ross and Tremblay, 2009; Tong et al., 2009; Tremblay et al., 2001; Tremblay and Kraus, 2002; Tremblay et al., 2010) as well as from mere passive exposure to repeated presentations of stimuli (Ross and Tremblay, 2009; Sheehan et al., 2005; Tremblay et al., 2010). Larger P2 amplitudes have also been associated with aging (Amenedo and Diaz, 1999; Ceponiene et al., 2008), but the literature is inconsistent, reporting also diminished or unchanged P2 amplitudes (for a review see Ceponiene et al., 2008).

To understand the functional significance of our finding in a group of unilateral hearing-aid users, it might be helpful to review the interpretations from different areas of research reporting enhanced P2 amplitudes and identify processes that could be

similar to the listening experience of the hearing-aid users, such as auditory training programs using discrimination or identification tasks to train their participants (Alain and Snyder, 2008; Ross and Tremblay, 2009; Tremblay and Kraus, 2002; Tremblay et al., 2009). All these studies reported an experience-related enhancement of P2 amplitudes that has been interpreted as reflecting enhanced arousal or awareness of trained stimuli. As P2 is thought to reflect the auditory-driven output of the mesencephalic reticular activating system (Crowley and Colrain, 2004), perhaps the training activates a preattentive alerting mechanism that contributes to improved perception.

The experience of a hearing-aid user that is exposed to new auditory stimuli made available through the hearing aid resembles the experience of auditory discrimination training, where new acoustic features are learned. In our study, only the unilaterally fitted hearing-aid users had significantly larger P2 amplitudes, but not the bilaterally fitted group. This finding suggests differences in the hearing experience of the two hearing-aid. If P2 reflects a preattentive alerting mechanism, then its enhancement could be related to the current hearing experience indicating that the unilateral group is more alerted – even under passive and non-demanding listening conditions as in our study – and directs more attention or processing resources to listening than normal-hearing people and bilaterally fitted hearing-impaired people.

Admittedly, this interpretation is speculative due to the cross-sectional design of our study without data on the dynamics of changes following hearing-aid fitting.

Longitudinal studies are needed that document the time course before hearing-aid provision and during a follow-up period of months or even years to elucidate further the plastic changes induced by amplification in the central auditory system.

A further characteristic of the P2 in our study was its scalp distribution with a significant P2 enhancement in the unilateral group at electrode site Pz only (Fig. 4), whereas the overall topographic distribution was similar for the three subject groups with maximum

values at Cz. In contrast, Tremblay and Kraus (2002) reported training-induced increases in P2 amplitude that were significant over both hemispheres across all midline and hemispheric recording sites. The authors questioned whether this widespread distribution of change of P2 suggests global rather than specific acoustic processes. The meaning of the parietal focus of P2 enhancement in the unilateral group in our study is unknown. Perhaps it also points to more general and modality-independent processes related to alertness and arousal.

Finally, an additional characteristic of the P2 in our study was the sustained double-peaked nature of P2 that was found in all three subject groups and was clearly visible in some traces (Figure 3). Our attempt to account for the double-peaked P2 by quantifying two subsequent portions of P2 over the latency range of the sustained positivity yielded a significant difference between the unilateral and bilateral groups for the early portion only, but not for the late. The latency windows for the early and late mean P2 amplitudes in our study were 130-240 ms and 240-350 ms, respectively. A similar double-peaked P2 has been described by Ceponiene et al. (2008) in a study on the effects of aging on auditory and visual processing. They found an age-related enhancement for both modalities in the later P2 range with a peak at about 250 ms. Regarding the auditory P2, they hypothesized that the late portion of P2 in the older group was caused by an overlap with a positivity not identical to the auditory P2 but similar to the positivity seen in the visual data. Ceponiene et al. (2008) did not provide an interpretation for the functional significance of the hypothetical late auditory P2 and the late visual P2 in the older group. However, the similarity of the auditory and visual P2 findings suggests a modality-independent underlying process.

In our study, a significant difference was found only for the early portion of P2 and between the two hearing-aid user groups. If the early P2 largely represents the "proper" auditory P2, then the difference between unilateral and bilateral hearing-aid users

could be related to more specific auditory processing differences and not to global modality-independent processes represented by the late portion of P2.

Even though the functional significance of the potentially two or more processes in the 130-350 ms latency window remains unknown, this latency range appears to be sensitive not only to the effects of aging (Ceponiene et al., 2008), but also of sensory acclimatization and deprivation. It may deserve more attention in future research.

Confounding factors

Several potentially confounding factors must be taken into account in the interpretation of our data. The unilateral group was older in age than the two other subject groups (77.1 vs. 69.6 and 70.1 years), and their overall duration of hearing-aid use was shorter than in the bilateral group (6.2 vs. 12.4 years). This imbalance reflects the prescription practice in Switzerland with different reimbursement criteria for the retired and working population. People who are employed are reimbursed for bilateral fittings, whereas people who are retired are reimbursed for one aid only. It cannot be excluded that the larger P2 of the unilateral group may be attributed partially to the older age rather than being a specific consequence of the unilateral fitting, or to the shorter overall duration of hearing-aid use. However, an aging effect is unlikely to account for the larger P2 in the unilateral group compared with the bilateral group since this would have also predicted a larger P2 in the unilateral group compared to the normal-hearing group, which was not observed.

Conclusions

The current study used late AEPs to investigate acclimatization effects following long-term unilateral hearing-aid use. A simple acclimatization effect with increased and

shorter responses for the aided ear compared to the unaided ear was not observed, but for P2 there was a significant interaction between ear and frequency indicating larger P2 amplitudes with the 2-kHz stimulus in the aided ear and larger P2 amplitudes with the 0.5- and 1-kHz stimuli in the unaided ear suggesting the presence of acclimatization. These results replicate and support the findings of Gatehouse and Robinson (1996) from a single subject.

P2 was also the only component of the P1-N1-P2 complex that appeared sensitive to capturing differences in central auditory processing between unilaterally and bilaterally fitted people. The double-peaked nature and sustained latency range of P2 suggests that two or more and possibly overlapping processes are contributing to this component representing both modality-specific auditory and more global modality-independent processes. The enhanced P2 amplitude in unilateral hearing-aid users in our study was interpreted as a potential correlate of more effortful auditory processing associated with the unilateral fitting compared to bilateral fitting. This interpretation is somewhat speculative and future research should explore further the functional significance of P2 in people with hearing impairment and try to untangle the presumed various and overlapping processes in the latency range of the sustained P2 component.

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754 **Figure captions**

755

756 **Figure 1:** Mean hearing thresholds (± 1 standard deviation) of right and left ears for the
757 bilaterally and unilaterally fitted hearing-aid users and for the normal-hearing controls.

758 **Figure 2:** Grand average waveforms of the three subject groups (unilateral, bilateral,
759 normal) for the 0.5 kHz stimulus presented at 85 dB SPL to the left ear at all eight
760 electrode sites.

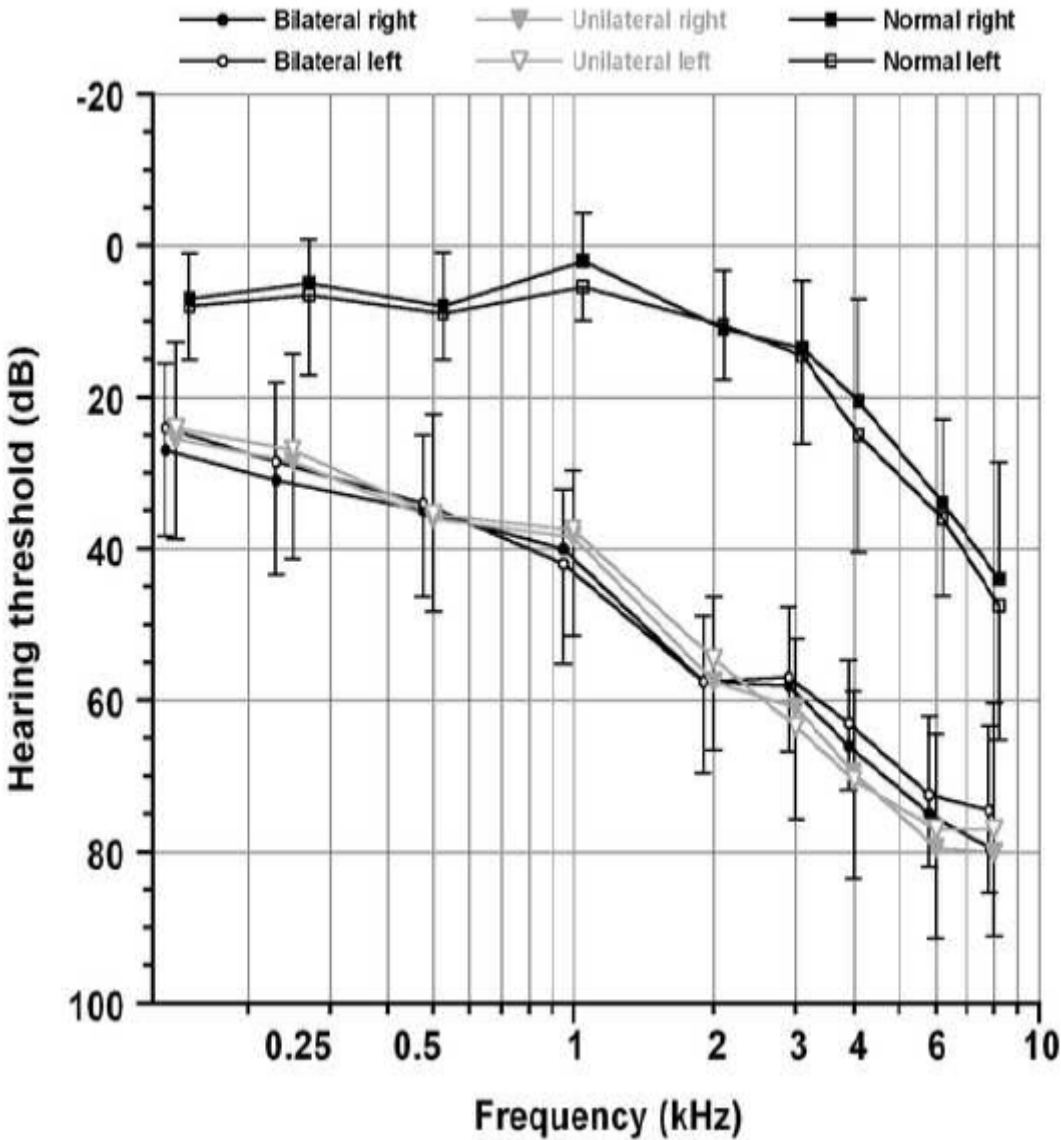
761 **Figure 3:** Grand average waveforms of the three subject groups (unilateral, bilateral,
762 normal) for all 18 conditions recorded at electrode sites Cz and Pz.

763 **Figure 4:** Mean P2 peak amplitudes (± 1 standard error) of the three subject groups
764 (unilateral, bilateral, normal) for the 18 conditions recorded at electrode sites Cz and
765 Pz.

766 **Figure 5:** Comparison of the AEPs from the aided versus unaided ear (for the unilateral
767 group) and from the left versus right ear (for the bilateral group) for the three
768 frequencies (0.5, 1, 2 kHz) and presentation levels (55, 70, 85 dB SPL) at electrode
769 site Cz.

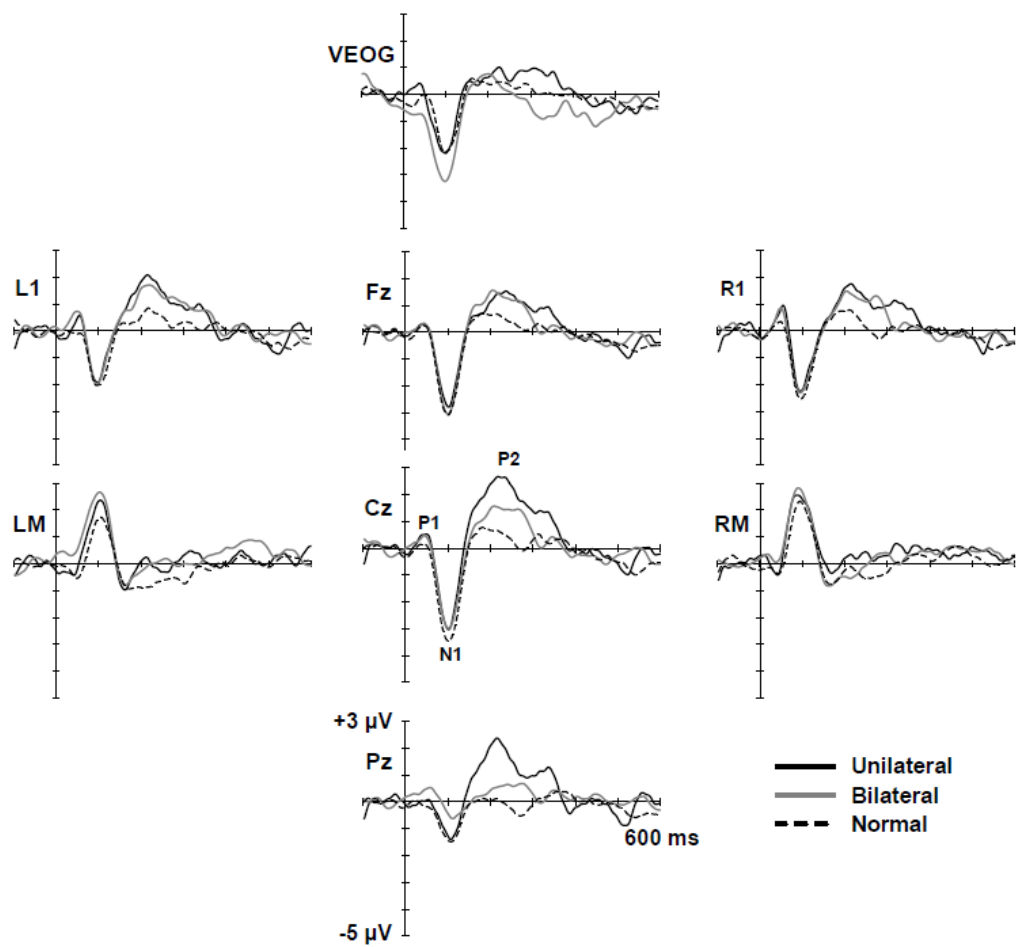
770 **Figure 6:** Mean P1, N1 and P2 peak amplitudes (left panel) and latencies (right panel)
771 at electrode site Cz plotted as a function of aided versus unaided ear (for the unilateral
772 group) and left versus right ear (for the bilateral group).

773 Figure 1:



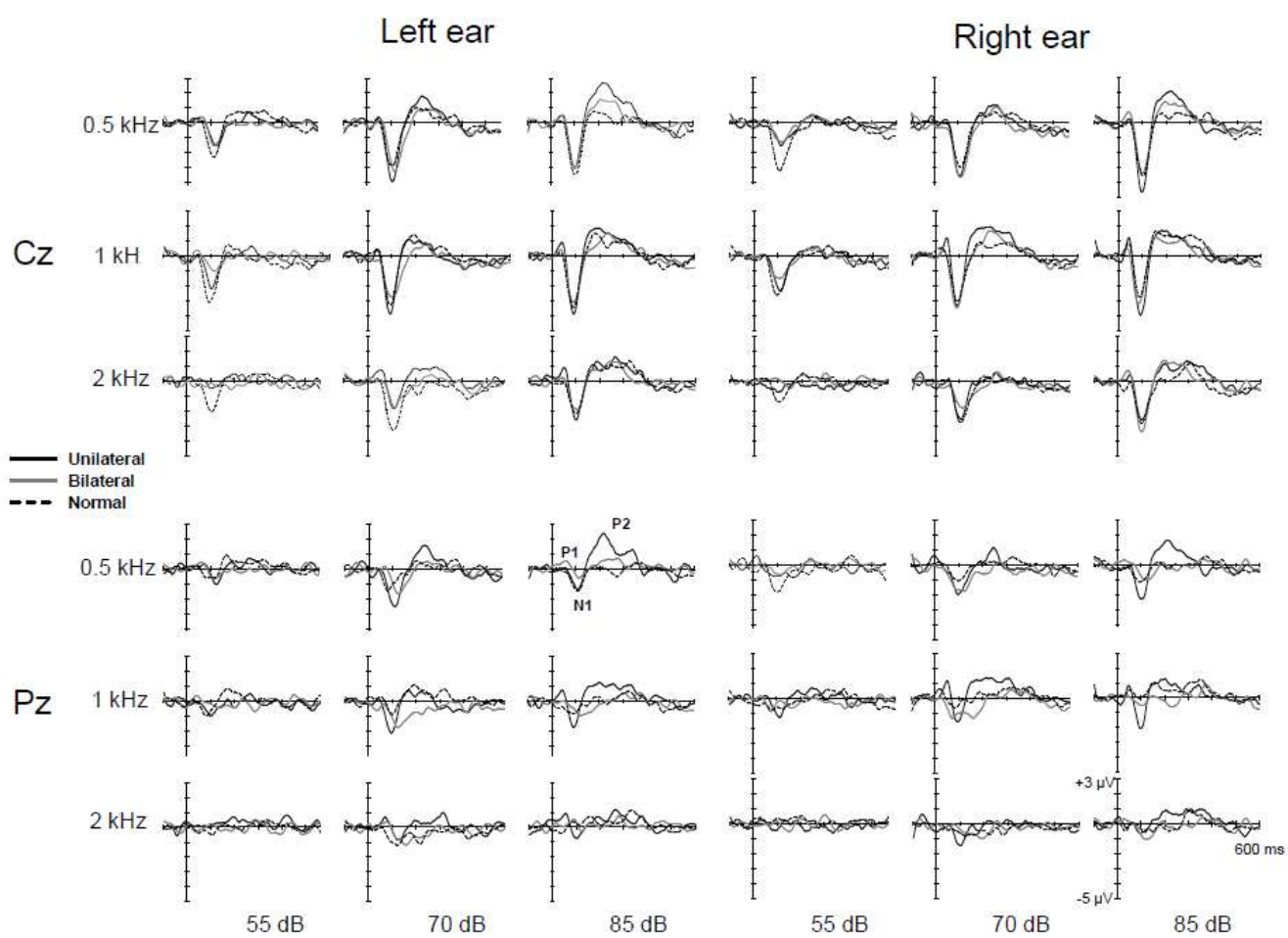
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775 Figure 2

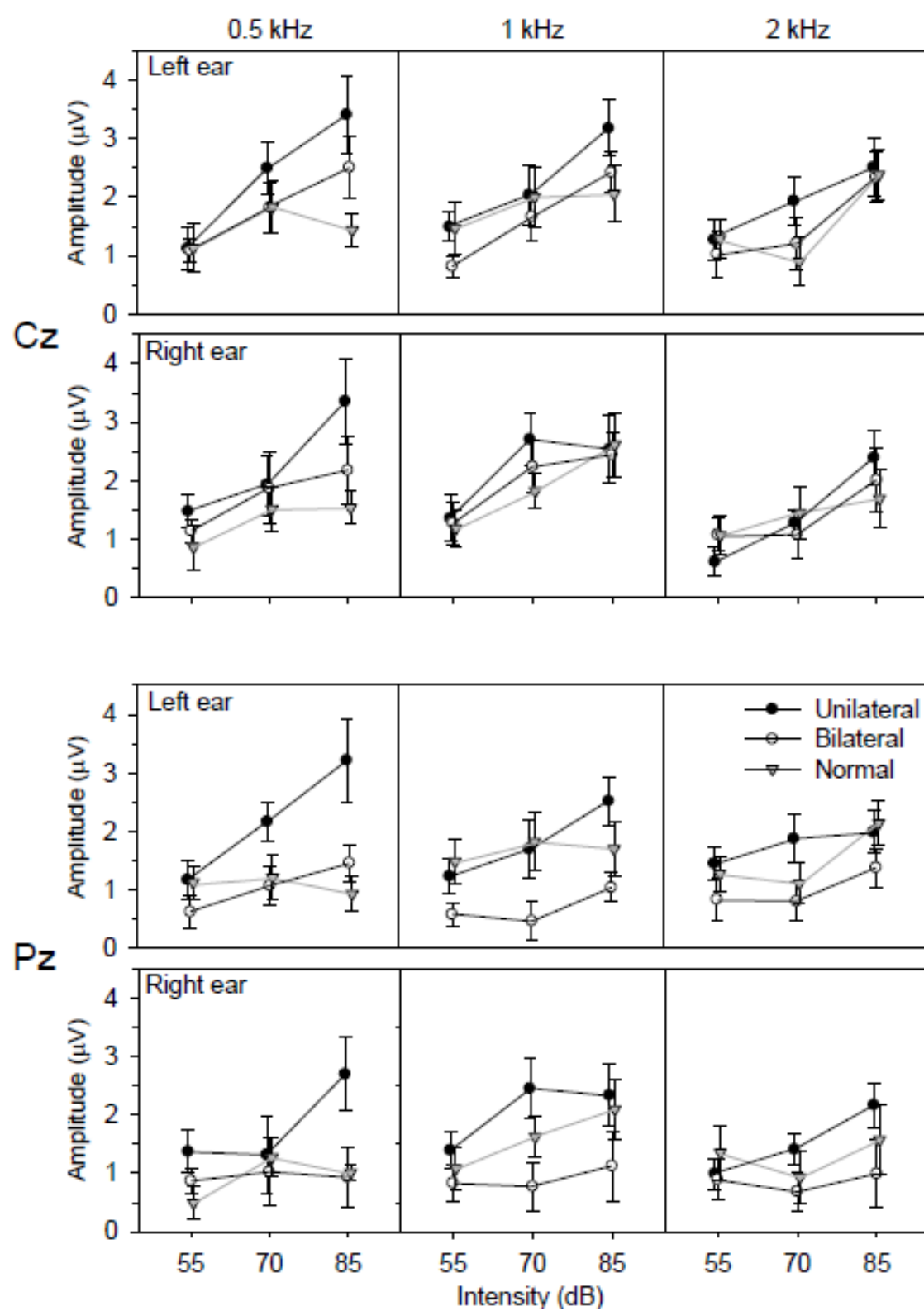


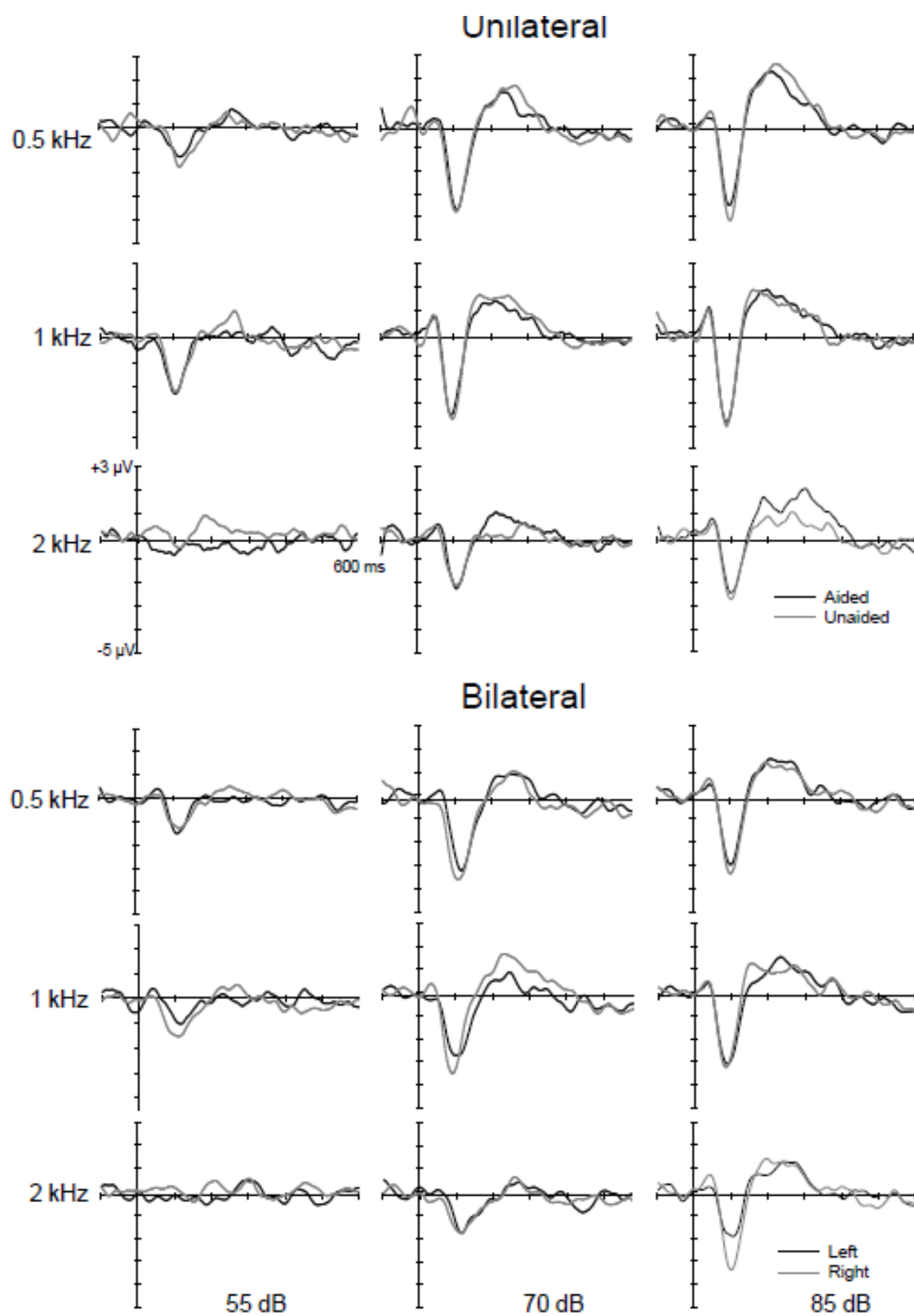
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777 Figure 3

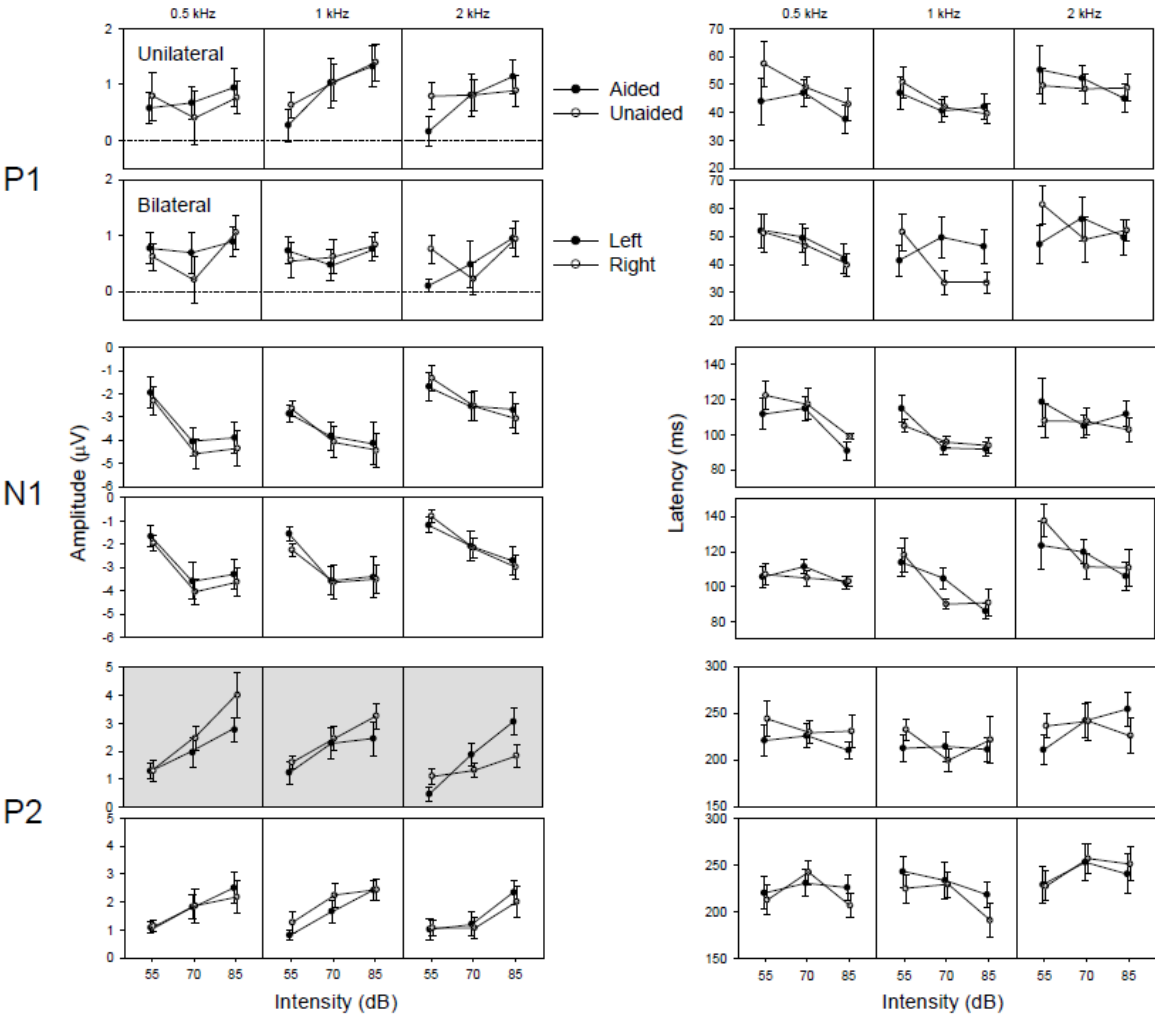


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783 Figure 6



784

Table 1: Results of speech audiometric tests. The ears of the normal and bilateral groups were grouped as left/right and the ears of the unilateral group as aided/unaided.

Subject group	50% speech discrimination (dB SPL)		S/N ratio SPIN-test (dB SPL)		Noise level SPIN-test (dB SPL)	
	Right/unaided ear	Left/aided ear	Right/unaided ear	Left/aided ear	Right/unaided ear	Left/aided ear
Normal	19.0 (SD 4.8)	21.4 (SD 5.1)	1.5 (SD 2.2)	1.8 (SD 1.0)	60.0	60.0
Bilateral	52.9 (SD 9.4)	53.9 (SD 9.9)	7.8 (SD 3.4)	7.2 (SD 3.2)	82.0 (SD 9.8)	83.0 (SD 10.3)
Unilateral	52.6 (SD 12.3)	56.7 (SD 10.1)	10.5 (SD 4.9)	7.6 (SD 4.8)	84.5 (SD 10.7)	84.0 (SD 8.8)

Table 2: F-values of repeated-measures ANOVAs for the AEP amplitudes and latencies at electrode sites Cz and Pz

Factor	df	Amplitudes					Latencies		
		P1	N1	P2	P2 _{early}	P2 _{late}	P1	N1	P2
Electrode site Cz									
Group (G)	2, 27	1.73	0.56	1.14	1.15	0.36	5.04*	3.59	1.05
Ear (E)	1, 27	0.00	3.19	0.69	2.20	0.00	0.16	0.05	1.67
Frequency (F)	2, 54	0.97	29.25***	6.27**	10.58***	2.56	11.96***	18.99***	3.69
Level (L)	2, 54	7.83**	20.51***	31.22***	23.60***	17.77***	0.57	17.18***	1.12
G x E	2, 27	0.22	2.43	0.55	1.04	0.88	0.42	0.76	3.07
G x F	4, 54	0.34	1.16	1.58	0.32	0.45	0.21	1.51	0.33
G x L	4, 54	1.80	2.04	1.36	1.49	0.98	0.94	0.95	0.47
G x E x F	4, 54	0.36	0.72	0.37	0.79	0.30	2.71	0.52	0.72
Electrode site Pz									
Group (G)	2, 27	0.66	0.57	5.43*	5.80**	2.17	0.19	2.07	0.81
Ear (E)	1, 27	0.02	0.58	0.92	1.96	1.40	0.57	0.03	0.00
Frequency (F)	2, 54	0.80	19.76***	0.81	2.31	1.31	4.40*	9.28**	0.53
Level (L)	2, 54	3.04	6.88**	13.81***	5.09*	4.55*	1.01	0.02	4.14*
G x E	2, 27	1.05	1.06	0.18	0.33	0.30	0.06	0.33	1.23
G x F	4, 54	0.52	0.91	2.99	1.37	0.87	0.68	0.51	0.58
G x L	4, 54	0.48	1.06	2.15	2.96	1.10	0.83	1.39	0.60
G x E x F	4, 54	1.00	0.14	0.23	0.56	0.27	1.52	1.38	0.60

* $p < 0.025$; ** $p < 0.01$; *** $p < 0.001$

Table 3: F-values of repeated-measures ANOVAs for the difference values of AEP amplitudes and latencies (unilaterally and bilaterally fitted group)

Factor	df	Amplitudes					Latencies		
		P1	N1	P2	P2 _{early}	P2 _{late}	P1	N1	P2
Electrode site Cz									
Group (G)	1, 18	0.10	0.01	0.60	0.17	0.05	1.02	0.00	1.66
Frequency (F)	2, 36	1.14	1.11	5.22*	1.83	2.60	0.66	0.37	0.67
Level (L)	2, 36	1.42	0.32	0.43	0.29	1.96	1.91	0.60	0.66
G x F	2, 36	0.07	0.11	2.27	0.91	0.29	1.38	1.22	1.25
G x L	2, 36	0.51	0.27	0.71	0.68	0.03	0.79	2.22	1.62
Electrode site Pz									
Group (G)	1, 18	1.28	0.03	2.55	1.05	0.91	1.69	1.92	0.02
Frequency (F)	2, 36	0.07	1.25	3.58	1.72	1.60	0.47	1.14	0.06
Level (L)	2, 36	0.72	0.15	0.11	0.11	1.03	0.47	0.30	0.26
G x F	2, 36	0.78	1.29	2.08	0.79	0.85	0.98	0.45	1.77
G x L	2, 36	0.01	0.26	1.57	1.28	0.39	1.20	0.89	0.30

* $p < 0.025$

Table 4: F-values of repeated-measures ANOVAs for N1, P2, composite N1-P2 peak amplitudes and P2 mean voltages at electrode sites Cz and Pz (unilaterally fitted group)

Factor	df	N1	P2	N1-P2	P2 _{early}	P2 _{late}
Electrode site Cz						
Ear (E)	1, 9	1.35	2.21	3.84	1.40	0.22
Level (L)	2, 18	8.93**	17.67***	23.36***	12.36**	12.57***
Frequency (F)	2, 18	11.32**	4.42	15.73***	3.82	2.24
E x L	2, 18	0.37	0.32	0.33	0.20	0.90
E x F	2, 18	0.45	6.1*	2.94	1.19	1.72
Electrode site Pz						
Ear (E)	1, 9	0.39	4.84	3.09	1.20	0.26
Level (L)	2, 18	3.08	9.45**	8.83**	5.88*	8.61**
Frequency (F)	2, 18	5.84*	1.48	13.8**	2.06	0.51
E x L	2, 18	0.24	0.81	1.01	0.62	0.05
E x F	2, 18	1.26	3.97	5.55*	1.29	1.36

* $p < 0.025$; ** $p < 0.01$; *** $p < 0.001$